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TUBERCLE BACILLI IN THE HEART CLOTS IN ACUTE MILIARY TUBERCULOSIS COMPLICATING CHRONIC LYMPHATIC-MYELOGENOUS LEUKEMIA *

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It has been shown by Wilson[1] that tubercle bacilli can be demonstrated in stained sections of blood and clots obtained at autopsy from the heart and great vessels of a case of acute miliary tuberculosis, but that, as already borne out by the clinical attempts to demonstrate tubercle bacilli in the blood by means of stained smears, culture, and animal inoculation, the number of bacilli in the circulating blood at any given moment is too small to be of any practical diagnostic value. The wide-spread dissemination of the lesions in the case studied, occurring as they did even in the bone marrow, and the very early stage (thromboses and focal necroses) of many of the lesions would seem to make it a case in which the maximal number of bacilli might be found in the blood stream. That so few (4 bacilli in one-tenth of the heart clots) were found in the heart blood at any given moment cannot be taken as an absolute index of the number of tubercle bacilli entering the blood stream from a primary focus. Rather may it show, what we already know experimentally, that tubercle bacilli entering the blood stream quickly disappear from the circulating blood. The clots and blood in the great veins and right heart should contain few bacilli, as they have dropped out of the blood during its arterial and capillary circulation. It is possible that in an ordinary case all the tubercle bacilli entering the pulmonary veins from a primary bronchial-gland focus, and passing into the arterial blood, might disappear from the venous blood by the time it reached the right heart. That this did not take place in the case described is demonstrated by the presence of bacilli in the right auricular clot, and the numerous tuberculous thrombi and hematogenous tubercles in the pulmonary vessels. Her estimate of the number of bacilli contained in the circulating blood is based solely on the number left in the venous blood after its return to the

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* Received for publication February 21, 1916.

[1] Jour. Infect. Dis., 1916, 19, p. 260.

heart. The small number of bacilli found there is more an index of the number dropping out of the blood stream than of the number entering it.

A better estimate of the degree of bacillemia in tuberculosis would be the examination of arterial blood and clots. Usually, however, the left ventricle and aorta are empty at autopsy, and the left auricle contains but a small amount of clot or blood. The problem can be approached, however, by the study of the bacillary content of the right heart in cases of miliary tuberculosis in which the primary focus is on the venous side of the circulation, as for instance in the cervical or mesenteric lymph nodes. We have recently had in this laboratory such a case, with primary tuberculosis of the cervical lymph nodes and an even more widely disseminated miliary tuberculosis (skin, endocardium) than in Wilson's case, with lesions in the same early stage. The case was one of chronic lymphatic-myelogenous leukemia with secondary tuberculosis.

THE CASE

A stationary engineer, aged 50 years, entered the clinic with a history of progressive enlargement of cervical lymph glands. On Sept. 10, 1915, an enlarged cervical gland was removed and sent to this laboratory for pathologic examination. Sections showed a lymphoid (aleukemic) hyperplasia strewn with young epithelioid noncaseating tubercles. During his stay in the hospital, up to his death on Oct. 11, 1915, a rapidly increasing number of white cells in the blood was observed; so that the final clinical diagnosis was given as acute miliary tuberculosis with acute leukemia.

The pathological diagnosis follows: Chronic lymphatic (mixed lymphatic-myelogenous) leukemia; primary tuberculosis of cervical glands; acute miliary tuberculosis of all organs, including skin; endocardial tubercles; multiple lymphomata of kidneys and liver; leukemic infiltrations of gallbladder and intestine; Roentgen-ray pigmentation of skin and atrophy of testes; chronic parenchymatous nephritis; chronic catarrhal gastritis; bronchopneumonia.

The marked lymphoid hyperplasia of lymph glands, particularly the cervical, the thickening of the capsule, the hyperplasia of the stroma and the periglandular infiltrations, the hyperplasia of the spleen and the bone marrow, the presence of lymphomata and leukemic infiltrations throughout the body—all indicate a chronic leukemic process. The early stage of the tuberculous lesions shows a later secondary infection beginning in the cervical glands and thence spreading by both hematogenous and lymphogenous metastases throughout the body. The small number of leukocytes in the circulating blood when the patient was first examined, could be explained as the result of a decrease caused by acute tuberculous infection (aleukemic stage). The increase in the number of leukocytes observed during the patient's stay in the hospital may be interpreted as a change from the aleukemic to the former leukemic condition, induced by the acute infection.

The right auricle and ventricle were dilated and partly filled with soft leukemic clots (chicken-fat clots), 90 c.c. in amount in all. Sixty cubic centimeters of the clot were fixed in alcohol and 30 c.c. in formol. A portion of the alcohol-fixed clot, measuring 9 by 6 by 0.45 mm. (24.3 c.mm.), was imbedded in paraffin, and cut into 60 sections, 7.5 microns each in thickness. These sections were floated onto warm carbolfuchsin, stained, decolorized, and washed without removing the paraffin, then floated onto slides, dried, the paraffin removed by warming and applying xylol, and the sections finally mounted in balsam.

The 60 stained sections were thoroughly studied in all parts on a movable stage. Only absolutely typical and unquestioned tubercle bacilli were counted. The fact that the clots were leukemic, made up almost entirely of white cells, with but few red cells and these hemolyzed by the alcohol fixation, made the search for tubercle bacilli much easier than was the case in formol-fixed clots. By means of the movable stage one slide could be thoroughly examined in 1 hour; 60 full hours were given to the examination of the 60 slides. Four absolutely typical tubercle bacilli were found which by size, morphology, and staining were identified beyond question; also 15 suspicious fragments, which were disregarded. The sections were well stained, contained little dirt, and few acid-resisting crystalline structures were to be seen. The 4 bacilli were in the focal plane of the section between the white cells, and could not have been technical artefacts or acid-resisting bacilli from water or air. They must have existed in the blood clot at the time of its formation. The portion of clot examined represented 0.027% of the entire clot obtained from the heart. An estimate of the number of bacilli occurring in the entire clot, should this ratio of occurrence persist throughout, would give 14,815 bacilli for the entire clot. Such a calculation, however, does not sufficiently consider the laws of chance, and must not be too strongly heeded. The fact remains that in a case of acute miliary tuberculosis 4 tubercle bacilli to 60 slides, or 1 to 15, were found in the venous blood of the right heart. This proportion, which is not uncommon in sputum examinations in incipient cases of pulmonary tuberculosis, or in examinations of urinary sediments, is not considered insignificant as a clinical diagnostic effort in such conditions.

Tubercle bacillemia is a common, if not universal, occurrence in cases of tuberculosis. Can it be demonstrated in blood drawn from the living patient? Probably only by examination of many slides, a laborious undertaking, perhaps more laborious and time-consuming than the examination of sputum and urinary smears in cases of suspected incipient pulmonary and renal tuberculosis, but nevertheless worth while in many cases. The examination of blood taken from the living patient will probably give results more frequently in cases in which the primary focus is in the lungs or bronchial nodes; while in the cadaver the heart blood of the right side will contain more bacilli in those cases in which the primary lesion is giving off bacilli to the venous circulation. The report of Brandes[2] on the examination of blood from 40 cases of surgical tuberculosis with positive results in 45% of these cases (5 c.c. of blood treated by the Schnitter-Uhlenhuth antiformin method) strengthens the belief that the attempt may not be as difficult as it now seems. A suggested improvement consists in imbedding in paraffin the sediment obtained by the antiformin method (decantation method of paraffin imbedding, as for blood), and the examination of the stained sections rather than smears. Thus some of the technical artefacts would be avoided and labor saved.

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[2] Deutsch. med. Wchnschr., 1913, 39, p. 1137.